

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	29221	mannos\$4	US-PGPUB; USPAT	OR	ON	2006/12/05 09:08
L2	410237	phosphate phospho phosphoryl\$8	US-PGPUB; USPAT	OR	ON	2006/12/05 09:08
L3	1830	1 near4 2	US-PGPUB; USPAT	OR	ON	2006/12/05 08:42
L4	125189	inflammatory inflammation	US-PGPUB; USPAT	OR	ON	2006/12/05 09:08
L5	51469	epithelial	US-PGPUB; USPAT	OR	ON	2006/12/05 09:08
L6	42130	vagina\$4 vaginitis	US-PGPUB; USPAT	OR	ON	2006/12/05 09:09
L7	1154	3 and (4 5 6)	US-PGPUB; USPAT	OR	ON	2006/12/05 08:43
L8	110	3 same (4 5 6)	US-PGPUB; USPAT	OR	ON	2006/12/05 08:43
L9	110	7 and 8	US-PGPUB; USPAT	OR	ON	2006/12/05 09:08
L10	3381	mannos\$4	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:08
L11	127724	phosphate phospho phosphoryl\$8	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:08
L12	74513	inflammatory inflammation	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:08
L13	6492	epithelial	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:09
L14	9451	vagina\$4 vaginitis	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:09
L15	338	10 and 11	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:09
L16	28	15 and (12 13 14)	EPO; JPO; DERWENT	OR	ON	2006/12/05 09:09

(FILE 'HOME' ENTERED AT 10:02:13 ON 05 DEC 2006)

FILE 'CAPLUS' ENTERED AT 10:02:25 ON 05 DEC 2006

L1 E YANG SHU/IN  
34 S E3 OR E15  
L2 E HUANG YANBIN/IN  
19 S E3  
E HUANG YAN/IN  
L3 51 S E3  
L4 6 S L1 AND (L2 OR L3)  
L5 39753 S MANNOSE  
L6 605488 S PHOSPHATE  
L7 1 S L4 AND L5 AND L6

FILE 'REGISTRY' ENTERED AT 10:09:47 ON 05 DEC 2006

L8 1 S MANNOSE 6-PHOSPHATE/CN  
L9 0 S MANNOSE 3-PHOSPHATE/CN  
L10 0 S MANNOSE 1-PHOSPHATE/CN  
L11 324 S C6 H13 O9 P/MF  
L12 6119 S MANNOSE  
L13 15 S L11 AND L12

FILE 'CAPLUS' ENTERED AT 10:14:14 ON 05 DEC 2006

L14 14 S L13/PAC  
L15 66 S L13/THU  
L16 1003 S L13/BIOL  
L17 1003 S L15 OR L16

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 10:16:17 ON 05 DEC 2006

FILE 'CAPLUS' ENTERED AT 10:16:52 ON 05 DEC 2006

L18 46857 S MANNOS?  
L19 605488 S PHOSPHATE  
L20 934 S L17 AND L18 AND L19  
L21 934 S L20 OR L17  
L22 1003 S L20 OR L17  
L23 21020 S VAGINA?  
L24 801 S VAGINITIS  
L25 17731 S ATROPHY  
L26 163511 S EPITHEL?  
L27 31 S L22 AND (L23 OR L24 OR L25 OR L26)  
L28 972 S L22 NOT L27  
L29 61 S L15 NOT L27  
L30 55 S L29 AND L18 AND L19 → D SCAN  
L31 6 S L29 NOT L30

=> S L22 NOT (L27 OR L29)

L32 911 L22 NOT (L27 OR L29)

=> S L32 AND L23

L33 0 L32 AND L23

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1004340 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 143:292562  
 TITLE: Mannose phosphate compositions for vaginal treatment  
 INVENTOR(S): Yang, Shu-ping; Huang, Yanbin  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 12 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203032	A1	20050915	US 2004-801063	20040315
WO 2005094840	A1	20051013	WO 2005-US772	20050106
WO 2005094840	C1	20060810		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-801063 A 20040315

OTHER SOURCE(S): MARPAT 143:292562

AB The invention provides mannose 6-phosphate and salts thereof for increasing vaginal cell growth, vaginal cell maturation and vaginal moisture, as well as compns., articles and methods for treating and preventing vaginal conditions characterized by poor vaginal cell growth, low vaginal cell differentiation and low vaginal moisture. Mannose-6-phosphate stimulated cell proliferation and vaginal cell maturation.

L27 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1004340 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 143:292562  
 TITLE: Mannose phosphate compositions for vaginal treatment  
 INVENTOR(S): Yang, Shu-ping; Huang, Yanbin  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 12 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005203032	A1	20050915	US 2004-801063	20040315
WO 2005094840	A1	20051013	WO 2005-US772	20050106
WO 2005094840	C1	20060810		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-801063 A 20040315  
 OTHER SOURCE(S): MARPAT 143:292562

AB The invention provides mannose 6-phosphate and salts thereof for increasing vaginal cell growth, vaginal cell maturation and vaginal moisture, as well as compns., articles and methods for treating and preventing vaginal conditions characterized by poor vaginal cell growth, low vaginal cell differentiation and low vaginal moisture. Mannose-6-phosphate stimulated cell proliferation and vaginal cell maturation.

L27 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:684077 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 143:302381

TITLE: Chlamydia pneumoniae uses the mannose 6-phosphate/insulin-like growth factor 2 receptor for infection of endothelial cells  
 AUTHOR(S): Puolakkainen, Mirja; Kuo, Cho-Chou; Campbell, Lee Ann  
 CORPORATE SOURCE: Department of Pathobiology, University of Washington, Seattle, WA, USA  
 SOURCE: Infection and Immunity (2005), 73(8), 4620-4625  
 CODEN: INFIBR; ISSN: 0019-9567  
 PUBLISHER: American Society for Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Several mechanisms for attachment and entry of Chlamydia have been proposed. We previously determined that the major outer membrane protein of Chlamydia trachomatis is glycosylated with a high-mannose oligosaccharide, and a similar structure inhibited the attachment and infectivity of C. trachomatis in epithelial cells. Because insulin-like growth factor 2 (IGF2) was shown to enhance the infectivity of Chlamydia pneumoniae but not C. trachomatis in endothelial cells, a hapten inhibition assay was used to analyze whether the mannose 6-phosphate (M6P)/IGF2 receptor that also binds M6P could be involved in infection of endothelial cells (HMEC-1) by Chlamydia. M6P and mannose 6-phosphate-poly[N-(2-hydroxyethyl)-acrylamide] (M6P-PAA) inhibited the infectivity of C. pneumoniae AR-39, but not C. trachomatis serovar UW5 or L2, while mannan inhibited the growth of C. trachomatis, but not C. pneumoniae. Using metabolically labeled organisms incubated with cells at 4° (organisms attach but do not enter) or at 37° (organisms attach and are internalized), M6P-PAA was shown to inhibit attachment and internalization of C. pneumoniae in endothelial

cells but did not inhibit attachment or internalization of *C. trachomatis* serovar E or L2. These findings indicate that *C. pneumoniae* can utilize the M6P/IGF2 receptor and that the use of this receptor for attachment and entry differs between *C. pneumoniae* and *C. trachomatis*.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:290472 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 140:264527  
 TITLE: Methods and compositions for treatment of neurological disorder  
 INVENTOR(S): Benowitz, Larry I.  
 PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA  
 SOURCE: PCT Int. Appl., 59 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004028468	A2	20040408	WO 2003-US30466	20030925
WO 2004028468	A3	20041021		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2499170	AA	20040408	CA 2003-2499170	20030925
AU 2003272728	A1	20040419	AU 2003-272728	20030925
EP 1542702	A2	20050622	EP 2003-754929	20030925
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1703227	A	20051130	CN 2003-825428	20030925
JP 2006503847	T2	20060202	JP 2004-540004	20030925
US 2005256059	A1	20051117	US 2005-528685	20050718
PRIORITY APPLN. INFO.:			US 2002-414063P	P 20020927
			WO 2003-US30466	W 20030925

AB The invention provides methods and compns. for producing a neurosalutary effect in a subject useful for the treatment of neurol. disorders, including retinal and optic nerve damage, in a subject in need thereof. The method includes administration to a subject a therapeutically effective amount of a hexose, such as mannose.

L27 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:678665 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 133:291537  
 TITLE: Insulin-like growth factor-II/cation-independent mannose 6-phosphate receptor mediates paracrine interactions during spermatogonial development  
 AUTHOR(S): Tsuruta, James K.; Eddy, E. M.; O'Brien, Deborah A.  
 CORPORATE SOURCE: The Laboratories for Reproductive Biology, Departments of Pediatrics, The University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA  
 SOURCE: Biology of Reproduction (2000), 63(4), 1006-1013  
 CODEN: BIREBV; ISSN: 0006-3363  
 PUBLISHER: Society for the Study of Reproduction  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The insulin-like growth factor-II/cation-independent mannose 6-phosphate (IGF-II/M6P) receptor transduces signals after binding IGF-II or M6P-bearing growth factors. It was hypothesized that this receptor relays paracrine signals between Sertoli cells and spermatogonia in the basal compartment of the seminiferous epithelium. For these studies spermatogonia were isolated from 8-day-old mice with purity

>95% and viability >85% after overnight culture. The IGF-II/M6P receptors were present on the surface of spermatogonia, as detected by indirect immunofluorescence. It was determined that both IGF-II and M6P-glycoproteins in Sertoli cell conditioned medium (SCM) modulate gene expression in isolated spermatogonia. The IGF-II produced dose-dependent increases in both rRNA and c-fos mRNA. These effects were mediated specifically by IGF-II/M6P receptors, as shown by studies using IGF-II analogs that are specific agonists for either IGF-I or IGF-II receptors. The SCM treatment also induced dose-dependent increases in rRNA levels, and M6P competition showed that this response required interaction with IGF-II/M6P receptors. The M6P-glycoproteins isolated from SCM by IGF-II/M6P receptor affinity chromatog. increased spermatogonial rRNA levels at much lower concns. than required by SCM treatment, providing further evidence for the paracrine activity of Sertoli M6P-glycoproteins. These results demonstrate that Sertoli cells secrete paracrine factors that modulate spermatogonial gene expression after interacting with cell-surface IGF-II/M6P receptors.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:257854 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 133:27118

TITLE: Involvement of insulin-like growth factors in early T cell development: a study using fetal thymic organ cultures

AUTHOR(S): Kecha, Ouafae; Brilot, Fabienne; Martens, Henri; Franchimont, Nathalie; Renard, Chantal; Greimers, Roland; Defresne, Marie-Paule; Winkler, Rosita; Geenen, Vincent

CORPORATE SOURCE: Institute of Pathology CHU-B23, University of Liege, Liege, B-4000, Belg.

SOURCE: Endocrinology (2000), 141(3), 1209-1217  
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The expression of insulin-like growth factor (IGF) and IGF receptor genes was investigated by RT-PCR during ontogeny of the murine thymus. IGF-1, IGF-1R, M6P/IGF-2R genes are expressed in the thymus both in fetal and postnatal life, whereas IGF-2 mRNAs decline after birth but are still detectable on the seventh week. By in situ hybridization, IGF-2 transcripts were located in the outer cortex and medulla of the postnatal thymus, and on the whole surface of the epithelial-like network in the fetal thymus. The effects of anti-IGFs and IGF-receptors neutralizing Abs on the generation of pre-T cell subpopulations were then investigated using fetal thymic organ cultures (FTOC). FTOC treatment with an anti-IGF-2 mAb, an anti-IGF-1R mAb, or an anti-M6P/IGF-2R polyclonal Ab induced a blockade of T cell differentiation at the CD4-CD8-stage, as shown by a significant increase in the percentage of CD4-CD8-cells and a decrease in the percentage of CD4+CD8+ cells. Moreover, anti-IGF-2 Ab treatment induced an increase in CD8+ cells suggesting that thymic IGF-2 might have a role in determining differentiation into the CD4 or CD8 lineage. Anti-IGF-1 Ab treatment decreased the proportion in CD4-CD8-cells and increased the frequency in CD4-CD8+. FTOC treatment with anti-(pro)insulin did not exert any significant effect on T cell development. These data indicate that the intrathymic IGF-mediated signaling plays an active role in the early steps of T cell differentiation during fetal development.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:811055 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 132:54839

TITLE: Cationic amphiphile micellar complexes for targeted gene or protein delivery

INVENTOR(S): Tousignant, Jennifer D.; Eastman, Simon J.; Chu, Quiming; Lee, Edward R.; Fang, Shaona L.

PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965461	A2	19991223	WO 1999-US13875	19990618
WO 9965461	A3	20000224		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2335638	AA	19991223	CA 1999-2335638	19990618
AU 9946984	A1	20000105	AU 1999-46984	19990618
EP 1085857	A2	20010328	EP 1999-930442	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002518313	T2	20020625	JP 2000-554341	19990618
PRIORITY APPLN. INFO.:			US 1998-89879P	P 19980619
			WO 1999-US13875	W 19990618

AB The effective introduction of foreign genes and other biol. active mols. into targeted mammalian cells is a challenge still facing those skilled in the art. Gene therapy, for example, requires successful transfection of target cells in a patient. The present invention relates to novel micellar complexes of cationic amphiphilic compds. that facilitate delivery of biol. active mols. to the targeted cells of a mammal. The novel micellar complexes are comprised of a cationic amphiphile, a biol. active mol., a derivative of polyethylene glycol (PEG), and optionally, a co-lipid. A further aspect of the invention is the use of targeting agents in any of the methods that effectuate the delivery of biol. active mols. into the cells of mammals. A targeting agent is usually any mol., peptide sequence, or large protein that preferentially targets or binds to specific mammalian cells.

L27 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:496035 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 131:267455

TITLE: Cellular Response to Latent TGF- $\beta$ 1 Is Facilitated by Insulin-Like Growth Factor-II/Mannose-6-phosphate Receptors on MS-9 Cells

AUTHOR(S): Ghahary, Aziz; Tredget, Edward E.; Mi, Lei; Yang, Liju

CORPORATE SOURCE: Department of Surgery, Wound Healing Research Group, University of Alberta, Edmonton, AB, T6G 2S2, Can.

SOURCE: Experimental Cell Research (1999), 251(1), 111-120  
CODEN: ECREAL; ISSN: 0014-4827

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study was conducted to explore the mechanism of activation of TGF- $\beta$ 1 which is critical to its role in many physiol. and pathol. conditions. We have previously demonstrated that latent TGF- $\beta$ 1 modulates ECM through interaction with IGF-II/M6P receptors on dermal fibroblasts. In this report, we provide evidence that large (270 kDa) but not small (46 kDa) M6P receptors facilitate the cellular response to LTGF- $\beta$ 1 released from genetically modified cells. As a source of LTGF- $\beta$ 1, PA317 cells were transfected with either pLin-TGF- $\beta$ 1 vector or pLin vector with no TGF- $\beta$ 1 insert using calcium phosphate precipitation. Conditioned medium from transfected cells was removed after 3 days and used to evaluate the latency and bioactivity of TGF- $\beta$ 1 using ELISA and mink lung epithelial cell growth inhibition assay, resp. The level of TGF- $\beta$ 1 was 20-fold greater (2142 vs. 102 pg/mL) in conditioned medium derived from pLin-TGF- $\beta$ 1-transfected cells than in that of controls. Various vols. of this conditioned medium were then used to treat MS-9, SR-2, and MS cells bearing the large, small, and no IGF-II/M6P receptors, resp., for 24 h. [3H]Thymidine incorporation, used as an index for cell proliferation, showed a markedly lower level of proliferation in MS-9 cells in response to a given concentration of LTGF- $\beta$ 1 than was seen in SR-2 and MS cells. Interestingly, under similar exptl. conditions, either addition of M6P at 1 mM concentration or anti-TGF- $\beta$ 1 antibody abrogated the MS-9 cell proliferative response to LTGF- $\beta$ 1. In contrast, the inhibitory response of these three cell strains to heat-activated conditioned medium was the same. As another measure of LTGF- $\beta$ 1-induced cellular response, the expression of mRNA for pro  $\alpha$ 1(I) of type I collagen was also evaluated. A marked increase in

expression of this transcript in MS-9 cells in response to LTGF- $\beta$ 1 was observed. To further examine the possible correlation between the large IGF-II/M6P receptors and cellular responses to LTGF- $\beta$ 1, expression of IGF-II/M6P receptors at the protein and mRNA levels were evaluated by ligand binding and RT-PCR, resp. Using 125I-IGF-II as a ligand, the number of specific IGF-II/M6P receptors was found to be threefold greater on MS-9 than on SR-2 and MS cells. This finding was consistent with the level of IGF-II/M6P receptor mRNA detected by RT-PCR in MS-9 cells. In conclusion, the result of this study shows a direct link between large but not small IGF-II/M6P receptors on MS-9 cells and their response to LTGF- $\beta$ 1.

(c) 1999 Academic Press.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:456601 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 131:209522

TITLE: The mannose 6-phosphate /insulin-like growth factor-II receptor is a substrate of type V transforming growth factor- $\beta$  receptor  
AUTHOR(S): Liu, Qianjin; Grubb, Jeffrey H.; Huang, Shuan Shian; Sly, William S.; Huang, Jung San  
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, St. Louis University School of Medicine, St. Louis, MO, 63104, USA

SOURCE: Journal of Biological Chemistry (1999), 274(28), 20002-20010

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The type V transforming growth factor  $\beta$  (TGF- $\beta$ ) receptor (T $\beta$ R-V) is a ligand-stimulated acidotropic Ser-specific protein kinase that recognizes a motif of SXE/S(P)/D. This motif is present in the cytoplasmic domain of the mannose 6-phosphate /insulin-like growth factor-II (Man-6-P/IGF-II) receptor. The authors have explored the possibility that the Man-6-P/IGF-II receptor is a substrate of T $\beta$ R-V. Purified bovine Man-6-P/IGF-II receptor was phosphorylated by purified bovine T $\beta$ R-V in the presence of [ $\gamma$ -32P]ATP and MnCl<sub>2</sub> with an apparent K<sub>m</sub> of 130 nM. TGF- $\beta$  stimulated the phosphorylation of the Man-6-P/IGF-II receptor at 0° in mouse L cells overexpressing the Man-6-P/IGF-II receptor and in wild-type mink lung epithelial (Mv1Lu cells) metabolically labeled with [32P]orthophosphate. The in vitro and in vivo phosphorylation of the Man-6-P/IGF-II receptor occurred at the putative phosphorylation sites as revealed by phosphopeptide mapping and amino acid sequence anal. TGF- $\beta$  stimulated Man-6-P/IGF-II receptor-mediated uptake (.apprx.2-fold after 12 h treatment) of exogenous  $\beta$ -glucuronidase in Mv1Lu cells and type II TGF- $\beta$  receptor (T $\beta$ R-II)-defective mutant cells (DR26 cells) but not in type I TGF- $\beta$  receptor (T $\beta$ R-I)-defective mutant cells (R-1B cells) and human colorectal carcinoma cells (R11-37 cells) expressing T $\beta$ R-I and T $\beta$ R-II but lacking T $\beta$ R-V. These results suggest the Man-6-P/IGF-II receptor serves as an in vitro and in vivo substrate of T $\beta$ R-V and that both T $\beta$ R-V and T $\beta$ R-I may play a role in mediating the TGF- $\beta$ -stimulated uptake of exogenous  $\beta$ -glucuronidase.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:364324 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 131:111897

TITLE: Insulin-like growth factor-II/mannose 6 phosphate receptors facilitate the matrix effects of latent transforming growth factor- $\beta$ 1 released from genetically modified keratinocytes in a fibroblast/keratinocyte co-culture system  
AUTHOR(S): Ghahary, Aziz; Tredget, Edward E.; Shen, Qiong  
CORPORATE SOURCE: Department of Surgery, Wound Healing Research Group, University of Alberta, Edmonton, AB, T6G 2B7, Can.  
SOURCE: Journal of Cellular Physiology (1999), 180(1), 61-70



CODEN: JCLLAX; ISSN: 0021-9541

PUBLISHER: Wiley-Liss, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB This study was conducted to explore the mechanism of activation of transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) which is critical to its role in many physiol. and pathol. conditions. To date, almost all reports concerning TGF- $\beta$ 1 activation delineated that release of mature TGF- $\beta$ 1 from latency associated protein (LAP) is required for its activation. We report that latent TGF- $\beta$ 1 (LTGF- $\beta$ 1) released from TGF- $\beta$ 1 genetically modified keratinocytes grown in the top chamber of a co-culture system functions as a fibrogenic factor through interaction with insulin-like growth factor-II/mannose 6-phosphate (IGF-II/M6P) receptors of human dermal fibroblasts grown in the lower chamber of this system. Following successful transduction, the pLin-LTGF- $\beta$ 1 vector was amplified in PA317 packaging cells which possess viral structural proteins for vector in the presence of neomycin. Conditioned medium derived from packaging cells containing competent viral particles was then used to transduce either keratinocytes or fibroblasts grown in the upper chamber of a co-culture system, in which a 0.4  $\mu$ m porous membrane separates the two chambers. In this way, LTGF- $\beta$ 1 produced by transduced cells in the upper chamber is released and diffuses into the lower chambers where dermal fibroblasts are grown. Conditioned medium from the lower chamber was removed 3 days later and used to evaluate the latency and bioactivity of TGF- $\beta$ 1 using ELISA and mink lung (Mv1Lu) epithelial growth inhibition assay. Cells were also harvested and used for RNA extraction. The results of these expts. showed that (1) the TGF- $\beta$ 1-LAP complex, which was latent in traditionally used mink lung growth inhibition assay, directly modulated the expression of collagenase, type I, and type III collagen mRNA by dermal fibroblasts; (2) this stimulation was inhibited by M6P in a dose-dependent manner; (3) the TGF- $\beta$ 1-LAP inhibits Mv1Lu epithelial cells only when this complex was incubated with cell membranes isolated from dermal fibroblasts; and (4) LTGF- $\beta$ 1 activation seems to occur through a conformational alteration rather than by release of the mature TGF- $\beta$ 1 from LAP in our co-cultured system. This conformational alteration seems to occur through the interaction of the TGF- $\beta$ 1-LAP complex with the IGF-II/M6P receptors. Thus, the quantity of IGF-II/M6P receptors is important in cellular response to LTGF- $\beta$ 1 in any physiol. and pathol. conditions.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:162111 CAPLUS <<LOGINID::20061205>>  
DOCUMENT NUMBER: 130:205904  
TITLE: Compacting nucleic acids for delivery to cells without aggregation  
INVENTOR(S): Hanson, Richard W.; Perales, Jose C.; Ferkol, Thomas W.  
PATENT ASSIGNEE(S): Case Western Reserve University, USA; Ohio University  
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 216,534, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 10  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5877302	A	19990302	US 1997-716415	19970212
WO 9525809	A1	19950928	WO 1995-US3677	19950323
W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT			
RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN: INFO.: US 1994-216534 B2 19940323  
WO 1995-US3677 W 19950323

AB Methods and reagents for compaction of DNA without causing significant

aggregation and that can be used to facilitate their uptake by target cells are described. The nucleic acids may be used in gene therapy. Cell targetting may be achieved by binding the compacted DNA to a cell-specific ligand. The nucleic acid is preferably compacted to <30 nm or no more than twice its theor. min. diameter. Conjugates of polylysine and galactopyranosyl phenylisothiocyanate were used to compact a plasmid carrying a factor IX gene under control of the PEP carboxykinase gene promoter. The compacted complexes were injected into rat livers and the rats expressed the gene for the duration of the experiment (140 days). Expression of the gene was induced by feeding a carbohydrate-free diet and the human protein could be detected in the blood. The transforming DNA was maintained as an episome. Expts. with report genes introduced into muscle cells showed that use of the complexes increased reporter gene expression by about 20-fold.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:126376 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 128:189187

TITLE: Delivery of nucleic acids to airway epithelial cells as complexes with glycosylated derivatives of polylysine

INVENTOR(S): Glick, Mary Catherine; Scanlin, Thomas F.; Kollen, Wouter J. W.

PATENT ASSIGNEE(S): Children's Hospital of Philadelphia, USA

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806869	A1	19980219	WO 1997-US14280	19970813
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5948681	A	19990907	US 1997-907673	19970808
AU 9740659	A1	19980306	AU 1997-40659	19970813
PRIORITY APPLN. INFO.:			US 1996-23941P	P 19960814
			US 1997-907673	A 19970808
			WO 1997-US14280	W 19970813

AB A method of introducing foreign DNA into animal cells in vivo, especially airway epithelial cells, as a complex with polylysine substituted with glycosyl residues is described. This can be used in methods of treating humans having respiratory disease by gene therapy. The preferred sugar for glycosidation of polylysine is lactose, although  $\alpha$ -glucose,  $\beta$ -galactose, mannose, mannose-6-phosphate, fucose, or N-acetylglucosamine may also be used. Fusogenic peptides may also be used in the complex to increase the efficiency of uptake. Preparation of a number of glycosylated polylysine derivs. is described. Optimization expts. using cultured CF/T43 cells and a luciferase reporter gene are reported. Binding of the complex to the airway epithelial cells may be by lectins on the surface of the cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:115860 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 126:209198

TITLE: Mannose-6-phosphate binding protein of tumor cells detected with synthetic oligosaccharide probes

AUTHOR(S): Abramenko, I. V.; Belous, N. I.; Gluzman, D. F.; Tearteash, T. V.; Bovin, N. V.

CORPORATE SOURCE: R.E. Kavetsky Institute of Experimental Pathology,

Oncology and Radiobiology, Academy of Sciences of Ukraine, Kiev, 252022, Ukraine  
 SOURCE: Eksperimental'naya Onkologiya (1996), 18(1), 26-29  
 CODEN: EKSODD; ISSN: 0204-3564  
 PUBLISHER: Institut Eksperimental'noi Patologii, Onkologii i Radiobiologii im. R. E. Kavetskogo NAN Ukrainy  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Using immunocytochem. methods and synthetic oligosaccharide probes, the presence of mannose-6-phosphate (M6P)-binding mols. on the surface and in the cytoplasm of human hemopoietic and epithelial cells was studied. M6P-binding mols. of human malignant transformed epithelial cells were identified. One was a 395 kD protein with Ca<sup>2+</sup>-dependent carbohydrate binding segment. The specificity of the M6P recognition was demonstrated by inhibition tests in the presence of excess of low mol. weight ligands. Preliminary data suppose its participation in the intracellular adhesion processes.

L27 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:444595 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 125:133589  
 TITLE: Coordinate expression of insulin-like growth factor II (IGF-II) and IGF-II/mannose-6-phosphate receptor mRNA and stable expression of IGF-I receptor mRNA during differentiation of human colon carcinoma cells (Caco-2)  
 AUTHOR(S): Hoeflich, Andreas; Yang, Yi; Rascher, Wolfgang; Blum, Werner F.; Huber, Stefan; Koepf, Gabriele; Kolb, Helmut J.; Kiess, Wieland  
 CORPORATE SOURCE: Children's Hospital, Justus Liebig Univ., Giessen, Germany  
 SOURCE: European Journal of Endocrinology (1996), 135(1), 49-59  
 CODEN: EJOEEP; ISSN: 0804-4643  
 PUBLISHER: Scandinavian University Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Insulin-like growth factor II (IGF-II) has been implicated in the differentiation of skeletal muscle cells. In this study the putative role of IGF-II in epithelial cell differentiation was investigated. The expression of IGF-II, IGF-I receptor and IGF-II/mannose-6-phosphate receptor (IGF-II/M6P receptor) mRNA during spontaneous differentiation of the colon carcinoma cell line Caco-2 was measured. In addition, differentiation of Caco-2 cells during the cell culture period (days 1-21 in culture) was studied in parallel using morphol. (light and SEM) and biochem. markers of growth (DNA, RNA and protein content), and  $\beta$ -actin mRNA and glyceraldehyde phosphate dehydrogenase expression was studied using linear regression anal. Expression of IGF-II mRNA and IGF-II/M6P receptor mRNA correlated significantly with the progress of differentiation, while the IGF-I receptor was stably expressed throughout the culture period and exhibited a crucial role for the survival of Caco-2 cells, as shown by blocking expts. employing the monoclonal anti-IGF-I receptor antibody alpha-IR3. We hypothesize that: IGF-II mRNA and IGF-II/M6P receptor mRNA are expressed in a coordinate fashion during the differentiation of Caco-2 cells: coordinate expression of IGF-II and of IGF-II/M6P receptor mRNA might point to a role for IGF-II as growth stimulant and for the IGF-II/M6P receptor for a regulator of IGF-II bioavailability in differentiating cells; alternatively, high IGF-II/M6P receptor mRNA and protein expression in differentiated cells but low IGF-II binding to the IGF-II/M6P receptor point to an important intracellular role of this receptor type in differentiated colon epithelial cells; the IGF-I receptor mRNA is stably expressed during the differentiation process of Caco-2 cells; the IGF-I receptor protein seems to be a prerequisite for the survival of Caco-2 cells.

L27 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:999100 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 124:51669  
 TITLE: Organ-specific binding system for  $\beta$ -galactosidase in the male reproductive tract  
 AUTHOR(S): Grimalt, P.; Barbieri, M. A.; Sosa, M. A.; Bertini, F.  
 CORPORATE SOURCE: Universidad Nacional de Cuyo, Mendoza, Argent.  
 SOURCE: International Journal of Andrology (1995), 18(5),

243-7  
CODEN: IJANDP; ISSN: 0105-6263

PUBLISHER: Blackwell  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB This study reports on the binding of  $\beta$ -galactosidase obtained from different organs of the rat urogenital tract to membranes of these organs. Homologous and cross binding saturation assays indicated that: (1) high-affinity sites that recognize fructose-6-phosphate derivs. (FPR) are present in spermatozoa from the rete testis, epididymal membranes and testes, although the latter may reflect binding to testicular spermatozoa; (2) the membranes of the other organs studied do not have FPR; (3) the FPR of the epididymis does not recognize enzymes purified from other organs of the reproductive tract. These results suggest that the FPR-binding system belongs to a peculiar transport route that permits maturing spermatozoa to acquire hydrolytic enzymes secreted by the epididymal epithelium. In the epididymis and seminal vesicles more than 50% of the enzymic activity of  $\beta$ -galactosidase was recovered in cytosol, suggesting that the enzyme is located mainly in the secretory fluid of these organs.

L27 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:943113 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 123:330830

TITLE: Sertoli cell-spermatogenic cell interaction: the insulin-like growth factor-II/cation-independent mannose 6-phosphate receptor mediates changes in spermatogenic cell gene expression in mice

AUTHOR(S): Tsuruta, James K.; O'Brien, Deborah A.  
CORPORATE SOURCE: Lab. Reproductive Biol., Univ. North Carolina, Chapel Hill, NC, 27599-7500, USA

SOURCE: Biology of Reproduction (1995), 53(6), 1454-64

CODEN: BIREBV; ISSN: 0006-3363

PUBLISHER: Society for the Study of Reproduction

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The insulin-like growth factor (IGF)-II/cation-independent mannose 6-phosphate receptor (CI-MPR) is a multifunctional receptor with distinct binding sites for IGF-II and mannose 6-phosphate (M6P)-bearing glycoproteins. The authors used the immediate-early response gene c-fos to assay early changes in gene expression in spermatogenic cells in response to ligands for this receptor that are present in the seminiferous epithelium. The authors confirmed that c-fos behaves as an immediate-early response gene in spermatogenic cells after stimulation of protein kinase C with phorbol ester or after intercellular calcium levels are raised with calcium ionophore. After determining that IGF-II mRNA is present in Sertoli cells, the authors treated spermatogenic cells with this growth factor and found that it increased c-fos mRNA levels in a dose-dependent manner. Similarly, Sertoli-cell-conditioned medium (SCM) caused a dose-dependent increase in c-fos levels in spermatogenic cells isolated from adult mice. This effect was inhibited in the presence of 5 mM M6P, demonstrating that this change in c-fos gene expression was mediated by the IGF-II/CI-MPR. In addition, SCM treatment of purified pachytene spermatocytes and round spermatids caused a dose-dependent increase in 18S rRNA levels that was completely abolished in the presence of M6P. The results provide direct evidence that IGF-II/CI-MPR ligands secreted by Sertoli cells can modulate gene expression in spermatogenic cells and strongly suggest that they are important in the regulation of spermatogenesis.

L27 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:556748 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 122:288897

TITLE: Receptors involved in carbohydrate binding modulate intestinal epithelial-neutrophil interactions

AUTHOR(S): Colgan, Sean P.; Parkos, Charles A.; McGuirk, Deidre; Brady, Hugh R.; Papayianni, Aikaterini A.; Frendl, Gyorgy; Madara, James L.

CORPORATE SOURCE: Dep. Anesthesia, Pathology Med., Brigham Women's Hosp., Boston, MA, 02115, USA

SOURCE: Journal of Biological Chemistry (1995), 270(18),

10531-9  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PUBLISHER: American Society for Biochemistry and Molecular Biology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Neutrophil (polymorphonuclear neutrophil) migration across epithelial barriers is a common morphol. feature of many diseases. Previous studies show that PMN-epithelial interactions are dependent on the PMN  $\beta$ 2-integrin CD11b/18; however, nothing is known about surface carbohydrates and PMN-epithelial interactions. Here we investigate the role of carbohydrates on PMN-epithelial interactions using PMN and cultured monolayers of the intestinal epithelial cell line T84. Addition of the carbohydrates mannose 6-phosphate (Man-6-P) and glucose 6-phosphate (Glu-6-P), but not fructose 1-phosphate (Fru-1-P) inhibited transmigration by  $\geq 70\%$ . Likewise, more complex carbohydrates, such as fucoidin and the Man-6-P-rich polysaccharide PPME selectivity inhibited PMN transepithelial migration. These carbohydrates were found to be inhibitory in the apical-to-basolateral direction as well as the basolateral-to-apical direction, indicating a lack of polarity. This panel of related carbohydrates, however, was not effective in modulating short-term adhesion of PMN to epithelial monolayers, indicating that carbohydrate ligands may modulate different steps in the transmigration cascade. Finally, addition of functionally inhibitory monoclonal antibodies specific for the selectins (CD62E, CD62L, and CD62P) revealed no observable effect on PMN transmigration. These studies suggest that cell surface carbohydrates may play a role in inflammatory processes of the intestine.

L27 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:677741 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 121:277741  
 TITLE: Specific mannose-6-phosphate receptor-independent sorting of pro-cathepsin D in breast cancer cells  
 AUTHOR(S): Capony, Francoise; Braulke, Thomas; Rougeot, Christian; Roux, Sylvie; Montcourrier, Philippe; Rochefort, Henri  
 CORPORATE SOURCE: Institute National Sante Recherche Medicale, Univ. Montpellier I, Montpellier, 34090, Fr.  
 SOURCE: Experimental Cell Research (1994), 215(1), 154-63  
 CODEN: ECREAL; ISSN: 0014-4827  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The secretion of pro-cathepsin D (pro-cath-D) in some human metastatic breast cancer cells (MCF7, MDA/MB231), contrary to normal mammary cells, is not increased by ammonium chloride treatment, indicating a mannose-6-phosphate-independent sorting to lysosomes. By studying a variety of cell lines and lysosomal enzymes, we show that secretion of newly synthesized pro-cath-D was not mediated by the 46-kDa mannose-6-phosphate receptor (MPR) and that its resistance to NH<sub>4</sub>Cl for secretion was specific to cath-D and not to other lysosomal enzymes. This resistance appeared to be correlated with the basal hypersecretion of pro-cath-D, but not with its overexpression. By contrast, pro-cath-D secretion was increased by NH<sub>4</sub>Cl in fibroblasts and nontumoral epithelial mammary cells, suggesting a specificity for cancer cells. Immunofluorescence staining showed that pro-cath-D, but neither cathepsin B nor  $\beta$ -hexosaminidase, accumulated in intracytoplasmic vesicles of cells treated with ammonium chloride. In pulse-chase expts. and by subcellular fractionation on Percoll gradient, cath-D was found to be sorted into dense lysosomes whether cells were treated or not by NH<sub>4</sub>Cl. Treatment of cells with NH<sub>4</sub>Cl, however, inhibited processing and maturation of pro-cath-D, which was also observed in light vesicles in the absence of NH<sub>4</sub>Cl. Part of pro-cath-D, but not processed enzyme, was also found to be membrane associated in saponin-permeabilized cells. We conclude that in breast cancer cells, the MPR-independent pathway of pro-cath-D to lysosome is predominant compared to normal cells and other lysosomal enzymes. This alternative pathway should therefore be considered, in addition to MPR, to explain pro-cath-D sorting and activation in breast cancer cells.

L27 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:667346 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 119:267346  
 TITLE: Mouse Sertoli cells secrete mannose 6-phosphate containing glycoproteins that are endocytosed by spermatogenic cells  
 AUTHOR(S): O'Brien, Deborah A.; Gabel, Christopher A.; Eddy, E. M.  
 CORPORATE SOURCE: Dep. Pediatr., Univ. North Carolina, Chapel Hill, NC, 27599-7500, USA  
 SOURCE: Biology of Reproduction (1993), 49(5), 1055-65  
 CODEN: BIREBV; ISSN: 0006-3363  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Sertoli cells were isolated from prepubertal mice and cultured in serum-free medium to determine whether they secrete glycoproteins containing mannose 6-phosphate (M6P). Assays of the conditioned medium for lysosomal enzyme precursors, which typically bear the M6P recognition marker, indicated that Sertoli cells selectively secreted  $\beta$ -N-acetylhexosaminidase and  $\alpha$ -mannosidase, but not  $\beta$ -glucuronidase or  $\beta$ -galactosidase. Sertoli cells were labeled metabolically with [35S]methionine and the conditioned medium was fractionated on a cation-independent M6P receptor affinity column. Most of the secreted proteins did not bind to the column (peak A); however, approx. 10% of the radioactivity eluted as a low-affinity fraction (peak B), and 5-11% of the recovered cpm bound to the column and were eluted with 2.5 mM M6P (peak C). The radiolabeled proteins in each fraction were analyzed by 1- and 2-dimensional electrophoresis and fluorog. Two protein bands with mol. wts. of 30,000 and 35,000 were present in peak B. Peak C contained  $\geq 10$  M6P-containing glycoproteins with mol. wts. of 30,000-135,00 and isoelec. points  $< 6.5$ . The 35,000-mol.-weight constituent prominent both in peaks B and C was identified as procathepsin L by immunopptn. with a specific antibody. When pachytene spermatocytes and round spermatids were cultured overnight in the presence of peak C glycoproteins radiolabeled with 125I, both germ cell types accumulated these Sertoli M6P-glycoproteins by a receptor-mediated process that was specifically inhibited by M6P. The Sertoli M6P-glycoproteins taken up by germ cells were processed to lower mol. weight forms. These results provide evidence that M6P receptors on the surface of spermatogenic cells endocytose secreted glycoproteins that are likely to be present in the seminiferous epithelium.

L27 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1993:552810 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 119:152810  
 TITLE: Expression of IGF-II/Man-6-P receptors on rat, rabbit, and human colon epithelial cells  
 AUTHOR(S): Pillion, Dennis J.; Grizzle, William E.; Yang, Maria; Meezan, Elias; Stockard, Cecil R.; Ganapathy, Vadivel; Leibach, Frederick H.; Myers, Russell B.; Haskell, Joyce F.  
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Alabama, Birmingham, AL, 35294, USA  
 SOURCE: American Journal of Physiology (1993), 264(6, Pt. 2), R1101-R1110  
 CODEN: AJPHAP; ISSN: 0002-9513  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Previous expts. from this laboratory have established the presence of receptors for insulin and insulin-like growth factor I (IGF-I) on apical membranes prepared from rabbit colon epithelial cells; however, no receptors for multiplication-stimulating activity (MSA), the rat peptide hormone equivalent of human IGF-II, were found in this tissue. In the current studies, radioligand binding assays, covalent crosslinking expts., and immunoblot analyses using a polyclonal rabbit antiserum that recognizes the IGF-II/mannose 6-phosphate (Man-6-P) receptor, all confirmed the presence of IGF-II/Man-6-P receptors on membranes prepared from rat and human colon epithelial cells. Exposure of rat colon epithelial cell membrane fractions to 5 mM Man-6-P before incubation with 125I-labeled IGF-II increased radioligand binding. Immunoblot anal. indicated that IGF-II/Man-6-P receptors were present in both unfractionated rat colon membranes and fractions enriched with apical membranes. Rabbit and human colon epithelial cells displayed a different pattern of receptor distribution than rat colon

epithelial cells, with more insulin receptors but relatively few IGF-II/Man-6-P receptors. Immunohistochem. studies using a rabbit polyclonal antiserum confirmed that IGF-II/Man-6-P receptors were present on both the apical and the basolateral surfaces of colon epithelial cells.

L27 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:514586 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 119:114586

TITLE: Correlation between mannose-6-phosphate/IGFII receptor and cathepsin D RNA levels by in situ hybridization in benign and malignant mammary tumors

AUTHOR(S): Zhao, Yong; Escot, Chantal; Maudelonde, Thierry; Puech, Carole; Rouanet, Philippe; Rochefort, Henri

CORPORATE SOURCE: Univ. Montpellier I, Montpellier, 34090, Fr.

SOURCE: Cancer Research (1993), 53(12), 2901-5

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors evaluated levels of mannose 6-phosphate /insulin growth factor-II receptor (M6P/IGFII-R) RNA in breast cancer tumors by quant. in situ hybridization using a computer-aided image analyzer and compared them to cathepsin D RNA and protein levels in the same tissues. Breast cancer cells expressed more cathepsin D and M6P/IGFII-R RNA than fibroblasts in the same tumors. The authors found that a significant increase of cathepsin D RNA and M6P/IGFII-R RNA in breast cancer cells compared to epithelial cells of benign mastopathies. There was a pos. correlation between M6P/IGFII-R and cathepsin D RNA levels measured on serial sections. This contrasted with the inverse relation of these 2 RNA species in breast cancer cell lines where estrogen down regulates M6P/IGFII receptor RNA levels. Moreover, in vivo the authors found no correlation between the M6P/IGFII-R RNA level and menopausal or estrogen receptor status, suggesting that the in vivo regulation of M6P/IGFII-R RNA differs from its in vitro regulation in cell lines. The M6P/IGFII-R RNA level was not correlated cathepsin D status, histol grade, and tumor size but was significantly higher in lymph node-pos. tumors. The M6P/IGFII-R could therefore be an addnl. parameter to predict aggressive breast cancers, complementing cathepsin D assays and other more classical prognostic parameters.

L27 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:191471 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 116:191471

TITLE: Mannose 6-phosphate receptors: potential mediators of germ cell-Sertoli cell interactions

AUTHOR(S): O'Brien, Deborah A.; Gabel, Christopher A.; Welch, Jeffrey E.; Eddy, E. M.

CORPORATE SOURCE: Dep. Pediatr., Univ. North Carolina, Chapel Hill, NC, 27599-7500, USA

SOURCE: Annals of the New York Academy of Sciences (1991), 637(Male Germ Cell), 327-39

CODEN: ANYAA9; ISSN: 0077-8923

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 113 refs., on: cell-cell interactions in the seminiferous epithelium; mannose 6-phosphate receptors (MPR); MPRs in isolated spermatogenic and Sertoli cells; MPR-mediated endocytosis in Sertoli and germ cells; and Sertoli cell secretion of MP-containing glycoproteins that are endocytosed by spermatogenic cells.

L27 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:422766 CAPLUS <<LOGINID::20061205>>

DOCUMENT NUMBER: 115:22766

TITLE: Selective internalization of the apical plasma membrane and rapid redistribution of lysosomal enzymes and mannose 6-phosphate receptors during osteoclast inactivation by calcitonin

AUTHOR(S): Baron, Roland; Neff, Lynn; Brown, William; Louvard, Daniel; Courtot, Pierre J.

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA

SOURCE: Journal of Cell Science (1990), 97(3), 439-47

CODEN: JNCSAI; ISSN: 0021-9533

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of inhibition of bone resorption by calcitonin were studied at the level of the osteoclast. Although not epithelial, the osteoclast is polarized with the secretion of newly synthesized lysosomal enzymes and of acid occurring specifically at the apical pole, facing the bone compartment. The membranes composing the apical (ruffled-border) and basolateral domains contain topol. restricted antigens, a 100 + 103 Mr lysosomal membrane protein and Na<sup>+</sup>,K<sup>+</sup>-ATPase, resp. Calcitonin induces a rapid (15-60 min) redistribution of the apical marker as well as of markers of the secretory compartment of the osteoclast (arylsulfatase and cation-independent mannose 6-phosphate (Man6P) receptors). The apical plasma membrane, in contrast to the basolateral membrane, is selectively internalized. This internalization leads to the disappearance of the ruffled border. The vesicular translocation of apical membranes is reminiscent of the events occurring in gastric oxyntic cells and in kidney tubule intercalated cells during the regulation of acid secretion. In parallel, the synthesis of both the lysosomal enzyme arylsulfatase and Man6P receptors is arrested. The products that were already present in the secretory pathway seem to be rerouted to intracellular vacuoles instead of being targeted to the plasma membrane, leading to marked accumulation of enzymes in the inhibited cells. These results suggest that the rapid inhibition of bone resorption by calcitonin involves the vesicular translocation of the apical membranes and the rapid arrest in the synthesis and secretion of lysosomal enzymes in osteoclasts.

L27 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:140322 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 114:140322

TITLE: Identification of endogenous sugar-binding proteins in the accessory sex glands of NMRI mice. A histochemical and biochemical study

AUTHOR(S): Sinowatz, F.; Gabius, H. J.; Hauke, C.; Breipohl, W.; Amselgruber, W.

CORPORATE SOURCE: Inst. Vet. Anat., Univ. Munich, Munich, W-8000/22, Germany

SOURCE: Histochemistry (1991), 95(4), 357-63

CODEN: HCMYAL; ISSN: 0301-5564

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The histotopog. distribution of carbohydrate-binding proteins in the prostate and seminal vesicle of sexually mature NMRI mice was investigated using a panel of fluorescein-isothiocyanate (FTC) labeled neoglycoproteins (chemical glycosylated bovine serum albumin (BSA) and asialoglycoproteins. Addnl., biochem. anal. using affinity chromatog. and SDS-gel electrophoresis was performed to purify and characterize the resp. proteins from the tissue. Histochem. results demonstrate the presence of endogenous receptors for the carbohydrate part of glycoconjugates in both glands. In the prostate a distinct staining was seen after incubation with melibiose-BSA-FTC, glucuronic acid-BSA-FTC, and asialofetuin-FTC (only in the ventral prostate). In the epithelium of the seminal vesicle a weak staining occurred after incubation with asialofetuin-FTC and maltose-FTC. In the stroma of both accessory sex glands a distinct binding of several (neo)glycoproteins specific for  $\beta$ -galactoside-binding proteins was observed which could be attributed to a  $\beta$ -galactoside-binding lectin. Biochem. anal. confirmed the presence of such a histochem. detectable activity. The carbohydrate-binding proteins of the stroma, which were obviously linked to the elastic fibers, may play a role in the organization of the extracellular matrix in the interstitium of the glands.

L27 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:39827 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 114:39827

TITLE: Pentose phosphate pathway in rat colonic epithelium

AUTHOR(S): Butler, R. N.; Arora, K. K.; Collins, J. G.; Flanigan, I.; Lawson, M. J.; Roberts-Thomson, I. C.; Williams, J. F.

CORPORATE SOURCE: Dep. Gastroenterol., Queen Elizabeth Hosp., Woodville South, 5011, Australia

SOURCE: Biochemistry International (1990), 22(2), 249-60



CODEN: BIINDF; ISSN: 0158-5231

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The maximum catalytic capacities of the reactions of the nonoxidative pentose pathway for the conversion of ribose 5-phosphate to hexose and triose phosphates by the proximal and distal colon under feeding and starvation regimes are among the highest in the animal body. The qual. presence of the oxidative pentose pathway was assessed by measurement of the C-1/C-6 ratio value of 1.67-1.82. Enzymes of the F-type and L-type pentose pathways are present in colonocytes, and their maximum catalytic activities in colonocyte cytosol are reported. The contribution of the F-type pentose cycle to the total glucose metabolism of colonocytes, measured by the specific yield method, is negligibly low (.apprx.1.5%). Colonic epithelial cells use glucose at a high rate (7.1  $\mu\text{mol}/\text{min}/\text{g}$  dry weight), and 79% of the glucose is converted to lactate. Arabinose 5-phosphate has an intermediary role in the formation of keto pentose, sedoheptulose, and hexose phosphates from ribose 5-phosphate by colonocyte cytosol. The intermediary and reaction products of [1- $^{13}\text{C}$ ]ribose 5-phosphate dissimilation by colonocytes is investigated by  $^{13}\text{C}$  NMR spectroscopy. The  $^{13}\text{C}$  positional isotope distributions show labeling of C-1 and C-3 of hexose 6-phosphates consistent with either the theor. predictions of the F-type pentose pathway or of the activities of exchange reactions catalyzed by transketolase and(or) transaldolase. Measurements of exchange reactions showed that the C-1/C-3 labeling of these compds. is mostly, if not wholly, attributable to exchange catalysis by these group-transferring enzymes. Apparently, the F-type PC has little role in the glucose metabolism of colonocytes, and pentose phosphate formation may thus occur by a contribution (.apprx.20% of the total glucose metabolism) by the alternate L-type pathway.

L27 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:495169 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 113:95169

TITLE: Surface distribution of the mannose 6-phosphate receptors in epithelial Madin-Darby canine kidney cells

AUTHOR(S): Prydz, Kristian; Braendli, Andre W.; Bomsel, Morgane; Simons, Kai

CORPORATE SOURCE: Eur. Mol. Biol. Lab., Heidelberg, D-6900, Germany

SOURCE: Journal of Biological Chemistry (1990), 265(21), 12629-35

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The surface polarity of both the cation-independent (CI-MPR) and the cation-dependent (CD-MPR) mannose 6-phosphate receptors was analyzed in the epithelial Madin-Darby canine kidney (MDCK) cell line grown on polycarbonate filters. The surface localization was studied by plasma membrane domain-sp. surface labeling methods and by confocal microscopy using MPR-specific antibodies. The CI-MPR was shown to be exclusively present on the basolateral cell surface. In contrast, the CD-MPR was expressed neither apically nor basolaterally. However, an intracellular pool of CD-MPR could be detected. In MDCKII-RCAr cells, cell surface CI-MPR was shown to recycle between the basolateral plasma membrane and the trans-Golgi network. After exogalactosylation, cell surface CI-MPR acquired sialic acid residues in a time-dependent manner. Furthermore, the basolateral CI-MPR was shown to be functional. Lysosomal enzymes, bearing the mannose 6-phosphate recognition marker, were taken up from the basolateral medium and endocytosed into the cells. Uptake of lysosomal enzymes from the apical side was insignificant and not MPR mediated. These results extend previous immunoelectron microscopic studies on the intracellular polarity of the CI-MPR (Parton, R. G., et al., 1989) which showed that the CI-MPR was present in basolateral early endosomes and in late endosomes but absent from apical early endosomes.

L27 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:109882 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 108:109882

TITLE: Mannose 6-phosphate receptors on the plasma membrane on rat retinal pigment epithelial cells

AUTHOR(S): Tarnowski, Betty I.; Shepherd, Virginia L.;  
McLaughlin, Barbara J.

CORPORATE SOURCE: Dep. Anat. Neurobiol., Univ. Tennessee, Memphis, TN,  
USA

SOURCE: Investigative Ophthalmology & Visual Science (1988),  
29(2), 291-7  
CODEN: IOVSDA; ISSN: 0146-0404

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The retinal pigment epithelium (RPE) phagocytizes the tips of photoreceptor outer segments (OS) during normal eye function. It is not known what ligand on OS is recognized by the RPE for removal from the interphotoreceptor matrix. It is possible that a sugar residue on a cell surface glycoconjugate of either the OS or RPE mediates the phagocytic interaction. Pinocytic expts. with a soluble mannose 6-phosphate ligand (125I-labeled mannosidase) showed that similar quantities of ligand were bound by RPE explants from Long Evans rat retinas and from Royal College of Surgeons (RCS/p+) rat retinas known to be defective in the phagocytosis of OS. The addition of mannose 6-phosphate reduced the total counts of bound  $\alpha$ -mannosidase by 23% in both normal and dystrophic RPE explants. Mannose 6-phosphate receptors were visualized on normal and dystrophic RPE plasma membranes by immunocytochem. techniques. Further, phagocytosis was studied by using phosphomannan-coated beads as phagocytic particles. Dystrophic RPE phagocytized phosphomannan-coated beads by a mannose 6-phosphate specific mechanism as shown by a significant reduction in the number of these coated beads taken up in the presence of the competing sugar. In contrast, normal RPE showed no uptake of phosphomannan-coated beads. Apparently, a mannose 6-phosphate receptor is on the apical plasma membrane of rat RPE. This receptor may not be involved in normal OS phagocytic recognition, but may function in the trafficking of lysosomal enzymes by RPE cells.

L27 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:92052 CAPLUS <LOGINID::20061205>>

DOCUMENT NUMBER: 108:92052

TITLE: The distribution of 215-kilodalton mannose 6-phosphate receptors within cis (heavy) and trans (light) Golgi subfractions varies in different cell types

AUTHOR(S): Brown, William J.; Farquhar, Marilyn Gist

CORPORATE SOURCE: Sect. Biochem., Mol. Cell Biol., Cornell Univ.,  
Ithaca, NY, 14853, USA

SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (1987), 84(24), 9001-5  
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The distribution of mannose 6-phosphate (Man-6-P) receptors for lysosomal enzymes was investigated in Golgi subfractions prepared from 3 different cultured cell lines. Total microsomal fractions from clone 9 hepatocytes, normal rat kidney, or CHO cells were subfractionated by flotation in sucrose d. gradients, which resolves Golgi membranes into heavy (cis), intermediate, and light (trans) subfractions. In all cases, the results for the distribution of the receptors in Golgi subfractions obtained by Golgi subfractionation in d. gradients and by immunoelectron microscopy were in agreement. In clone 9 cells, Man-6-P receptors were enriched in heavy (cis) Golgi subfractions, whose peak d. ( $\rho = 1.17$ ) was greater than those containing either galactosyltransferase activity, a trans Golgi marker, or  $\alpha$ -mannosidase II, a middle Golgi marker. By immunoelectron microscopy, the receptors were localized to a single cis Golgi cisterna. In CHO cells, Man-6-P receptors were concentrated in Golgi membranes of low d. (1.12 g/mL) overlapping the peak of galactosyltransferase activity. By the immunoperoxidase technique, the receptors were usually localized to a single trans Golgi cisterna. In normal rat kidney cells, Man-6-P receptors were broadly distributed across Golgi membranes ( $\rho = 1.12$ -1.17), and by immunoperoxidase localization they were found to be broadly distributed across the stacked Golgi cisternae. Thus, the distribution of Man-6-P receptors within the Golgi complex varies from 1 cell type to another. These differences in receptor distribution may reflect variations in lysosomal enzyme trafficking among different cell types.

L27 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:99895 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 106:99895

TITLE: Extracellular release of acid hydrolases from cultured retinal pigmented epithelium

AUTHOR(S): Wilcox, David K.

CORPORATE SOURCE: Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15213, USA

SOURCE: Investigative Ophthalmology &amp; Visual Science (1987), 28(1), 76-82

CODEN: IOVSDA; ISSN: 0146-0404

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The intracellular and extracellular distribution of acid hydrolases in cultured retinal pigmented epithelium (RPE) was studied. Incubation of cultured RPE in medium containing 20 mM mannose 6-phosphate resulted in the extracellular release of .apprx.15% of the cell-associated activity of several acid hydrolases. This represented an .apprx.120% increase over control levels after 24 h of culture with 20 mM mannose 6-phosphate. The extracellular release was not due to cell lysis, since no release of the cytoplasmic marker lactate dehydrogenase was seen. N-Acetyl- $\beta$ -glucosaminidase,  $\alpha$ -mannosidase, and  $\beta$ -glucuronidase were released into the extracellular medium, whereas acid phosphatase and  $\beta$ -glucosidase were not. The release was specific for mannose 6-phosphate and was dose dependent. Inhibition of protein synthesis by treatment of RPE cells with cycloheximide (100  $\mu$ g/mL) inhibited extracellular acid hydrolase release. RPE cells exhibited N-acetyl- $\beta$ -glucosaminidase bound to the cell surface via a mannose 6-phosphate-sensitive receptor. Apparently, a specific extracellular release of acid hydrolases by RPE occurs and  $\geq 1$  acid hydrolase exists on the RPE cell surface. This may represent a mechanism for control of cell surface and extracellular levels of these enzymes in RPE via the mannose 6-phosphate receptor.

L27 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:82626 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 100:82626

TITLE: Enhancement of bacterial adhesion by shear forces: characterization of the hemagglutination induced by *Aeromonas salmonicida* strain 438

AUTHOR(S): Brooks, D. E.; Trust, T. J.

CORPORATE SOURCE: Dep. Pathol., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.

SOURCE: Journal of General Microbiology (1983), 129(12), 3661-9

CODEN: JGMIAN; ISSN: 0022-1287

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Application of a viscometric assay to the hemagglutination induced by *A. salmonicida* strain 438 showed that shear forces can enhance the strength of bacterial adhesion. The D-mannose/L-fucose-sensitive reaction proceeded in 2 phases, an initial phase in which the degree of aggregation remained constant during shearing and a 2nd stage, induced by shear, in which agglutination was enhanced as shear was maintained. The results strongly paralleled those found in studies of concanavalin A-induced hemagglutination, providing good evidence that adhesion in this species took place via lectin-like mols. Me  $\alpha$ -D-mannoside, which strongly inhibits hemagglutination in this system, would not fully reverse the shear-dependent reaction. EGTA inhibited and reversed both phases, however. The effects of bacterial concentration, temperature, time of growth, pH, and a spectrum of monosaccharide inhibitors were also studied. The results demonstrated that the shear-dependent reaction has a number of features which distinguish it from the initial stage of hemagglutination, implying differences in the underlying biochem. mechanisms involved.

L27 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1980:3682 CAPLUS &lt;&lt;LOGINID::20061205&gt;&gt;

DOCUMENT NUMBER: 92:3682

TITLE: Inhibition of lysosomal enzyme endocytosis by carbohydrate and lectins

AUTHOR(S): Von Figura, Kurt; Ullrich, Kurt; Mersmann, Guenther; Beeck, Hannelora; Weber, Ernst; Strecker, Gerard

CORPORATE SOURCE: USA  
 SOURCE: Glycoconjugate Res., Proc. Int. Symp., 4th (1979), Meeting Date 1977, Volume 2, 951-3. Editor(s): Gregory, John D.; Jeanloz, Roger W. Academic: New York, N. Y.  
 CODEN: 41RSAU  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB Lysosomal enzyme endocytosis by fibroblasts and liver epithelium occurs by binding to cell surface receptors which can also be recognized by specific saccharides, saccharide derivs., and lectins. Adsorptive endocytosis of lysosomal  $\alpha$ -N-acetylglucosaminidase;  $\beta$ -N-acetylglucosaminidase, arylsulfatase A, and  $\alpha$ -mannosidase was specifically and competitively inhibited by D-mannose, L-fucose, Me  $\alpha$ -D-mannopyranoside, p-nitrophenyl  $\alpha$ -glycosides of D-mannose and L-fucose, D-lyxose, D-arabinoside, and mannose 6-phosphate, all of which exerted inhibition by interaction with the cell surface receptor. On treatment of the lysosomal enzymes with alkaline phosphatase adsorptive endocytosis was inhibited or moderated for both fibroblasts and liver epithelium cells, indicating that the cell surface receptor recognizes a phosphorylated carbohydrate on lysosomal enzymes.  $\beta$ -Glucuronidase accumulation, the uptake of which was not affected by sugars, was not inhibited by alkaline phosphatase treatment. On pretreatment of fibroblasts with concanavalin A and wheat germ agglutinin, nonspecific inhibition of enzyme endocytosis was observed. This probably results from the effect of lectins on the lateral mobility of cell surface receptor components. Apparently, the receptor is a glycoprotein and(or) closely coupled to a lectin receptor.

L27 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1979:52165 CAPLUS <<LOGINID::20061205>>  
 DOCUMENT NUMBER: 90:52165  
 TITLE: Epithelial rat liver cells have cell surface receptors recognizing a phosphorylated carbohydrate on lysosomal enzymes  
 AUTHOR(S): Ullrich, Kurt; Mersmann, Guenther; Fleischer, Martin; Von Figura, Kurt  
 CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Muenster, Muenster, Fed. Rep. Ger.  
 SOURCE: Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1978), 359(11), 1591-8  
 CODEN: HSZPAZ; ISSN: 0018-4888  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Receptor-mediated endocytosis of  $\alpha$ -N-acetylglucosaminidase by cultured epithelial liver cells of rat was inhibited by mannose, L-fucose, and most effectively by mannose 6-phosphate. Endocytosis of  $\alpha$ -N-acetylglucosaminidase was lost after treatment of the enzyme with alkaline phosphatase. Apparently, rat epithelial liver cells possess cell surface receptors that recognize a phosphorylated carbohydrate on  $\alpha$ -N-acetylglucosaminidase, as was previously reported for cell surface receptors of human skin fibroblasts. Inhibition of  $\alpha$ -mannosidase endocytosis by rat epithelial liver cells in the presence of mannose 6-phosphate and loss of enzyme endocytosis after treatment with alkaline phosphatase suggest that this enzyme is recognized by the same receptor.